

Details of HPV-based Cervical Cancer Screening in Turkey

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Cervical Cancer in Turkey

- Incidence: 4-5 /100.000 (Years 2004-2015)
- Annual New Cases: 1.800
- 9. ranking among females
- Life time Risk: 0.55%
- Mortality Rate: 2 /100.000
- Stage Distribution
 - 55% Have Advanced Disease

Country	5 yrs Relative Survival % (Reference Year)
Turkey	62 (2009)
USA	68 (2006-2012)
UK	59 (2005-2007)
Germany	65 (1997-2006)
France	61 (2000-2007)
EU-28	62 (2000-2007)
Australia	72 (2008-2012)
Canada	73 (2006-2008)
Korea	80 (2008-2012)
China	74 (2005-2010)
Japan	72 (2003-2005)



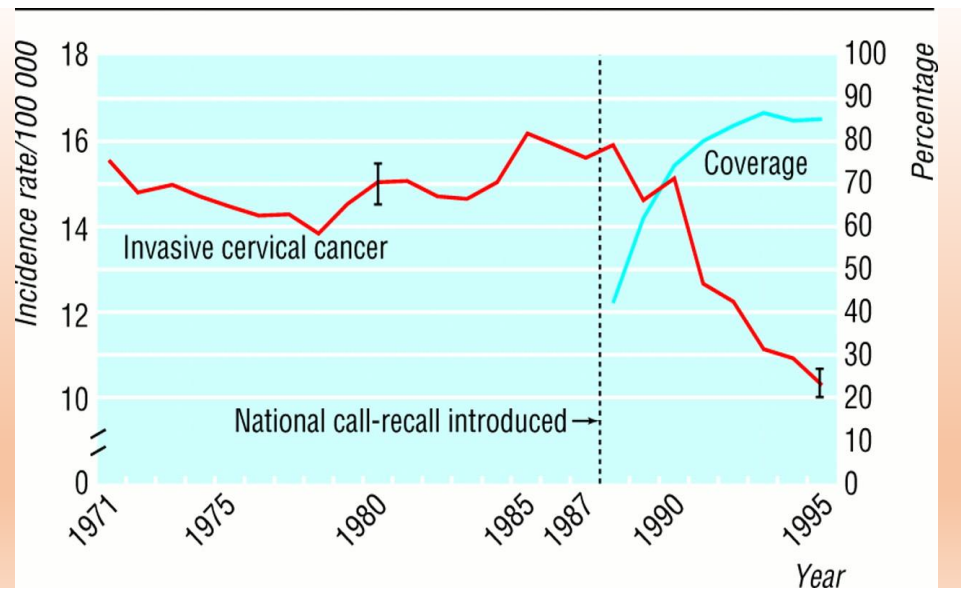
Cervical Cancer Globally

- ✓ Half Million New Cases
- ✓ 50% Mortality
- ✓ >90-99.7 % HPV Related
- ✓ Preventable Cancer
 - ✓ HPV Vaccination, Smoking Cessation
- ✓ Early Detection is Possible
 - ✓ VIA-VILI / Smear / HPV / Combination / Others
 - ✓ WHO
- ✓ Eradicable Cancer



Cervical Cancer Last Century

UK National Screening Programme



- ✓ Cytology based screening programs have reduced more than 75% of incidence and mortality from cervical cancer in the last 50 years.
- ✓ Especially in developed countries.
- ✓ However, **only 12** countries have succeeded in EUROPE (2017).
- ✓ And still cervical cancer mortality does not decrease any more **even in most developed** countries.



Cytology Based Screening: International Problems



✓ Scientific Problems

- A single Pap-Test has a very low sensitivity for CIN2+ lesions
- Pap-Test has a high false negative rate
- Reproducibility of Pap-Test is low
- Pap-Test is less effective in detecting adenocarcinoma of cervix

✓ Organisational Problems

- It is a very difficult and complex service to provide.



Previous Turkish Screening Program

✓ Pap-Smear since 1985, Population Based Since 2004

- KETEM + GP + Gynecologists
 - However, coverage rates could not exceed
 - 2% for population, 40% for opportunistic plus population based

Reason: Organisational Problems

- Large target population (15 Million)
- Lack of manpower (technician, expert)
- Frequent positional changes in manpower
- Lack of awareness (medical staff and population)
- Geographical limitations (large surface area, seasonal difficulties, transport difficulties)
- Quality control



Why HPV For Turkey ?

- ✓ For Screening Program Directors
 - Higher sensitivity
 - High Negative Predictive Value and Longer Screening Intervals
 - Low HPV positivity (low prevalence)
- ✓ For Academicians
 - Manpower advantage
 - Central quality control and automatization
- ✓ For Ladies
 - Shortening the time to final diagnosis
 - Self-testing ability for future a new test for ladies attention



Step By Step Turkish Implementation

- ✓ National and international consultations
- ✓ Pilot studies
- ✓ Preparation of legislations
- ✓ Family physicians in-service training and motivation of FP and patients
- ✓ National ID number based smart software



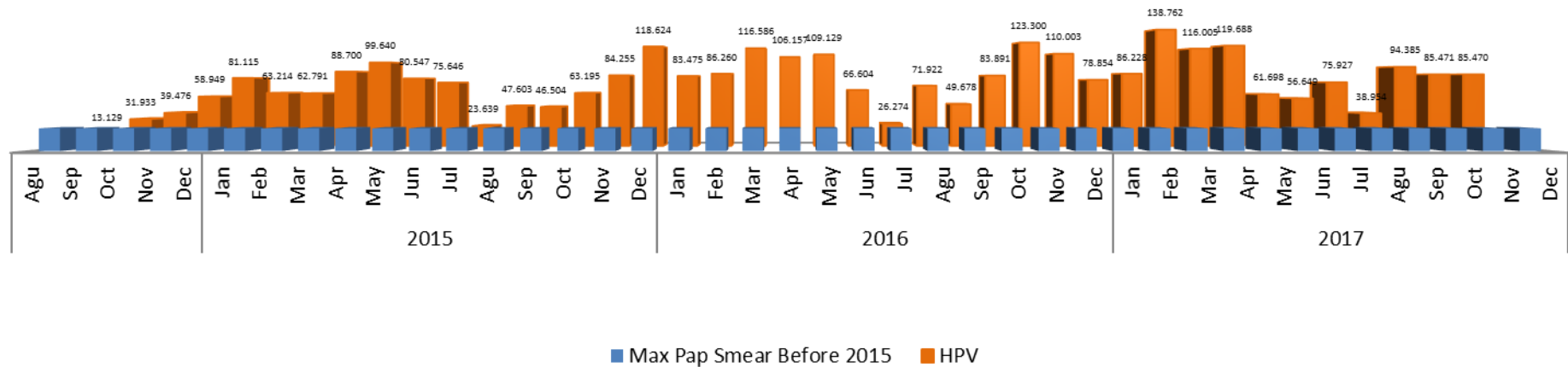
New Screening Program

- ✓ HPV + Conventional Smear in each five years, for women aged 30-65 years old
- ✓ GP & Nurses
 - 500 / GP or nurse for 5 Years, 10 /month
- ✓ Cargo to Ankara and Istanbul HPV Lab
- ✓ Results are on internet in 10 days maximal
- ✓ HPV Negative, nothing more
- ✓ HPV Positive, Genotyping Plus Double Blind Smear Evaluation
- ✓ Samples are stored for five years, smear pictures are also digitally stored
- ✓ Colposcopy Referral
 - HPV 16/ 18/ Other HPV with Cytological Abnormalities
 - Other HPV with NILM : 1 year later re-screen

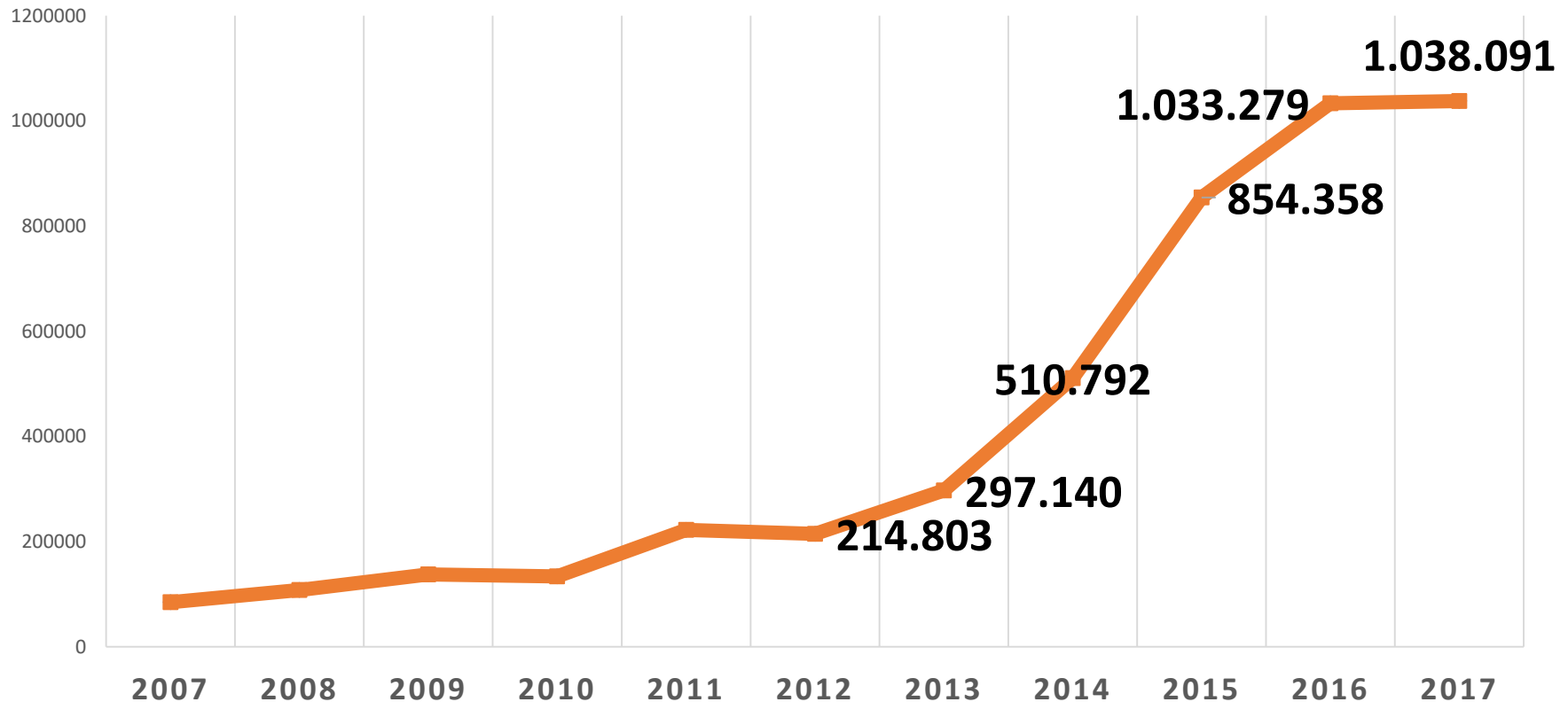


Role of HPV in Primary Level Screening

(Per Month; HPV DNA Screening vs. Max Pap-Smear Numbers)

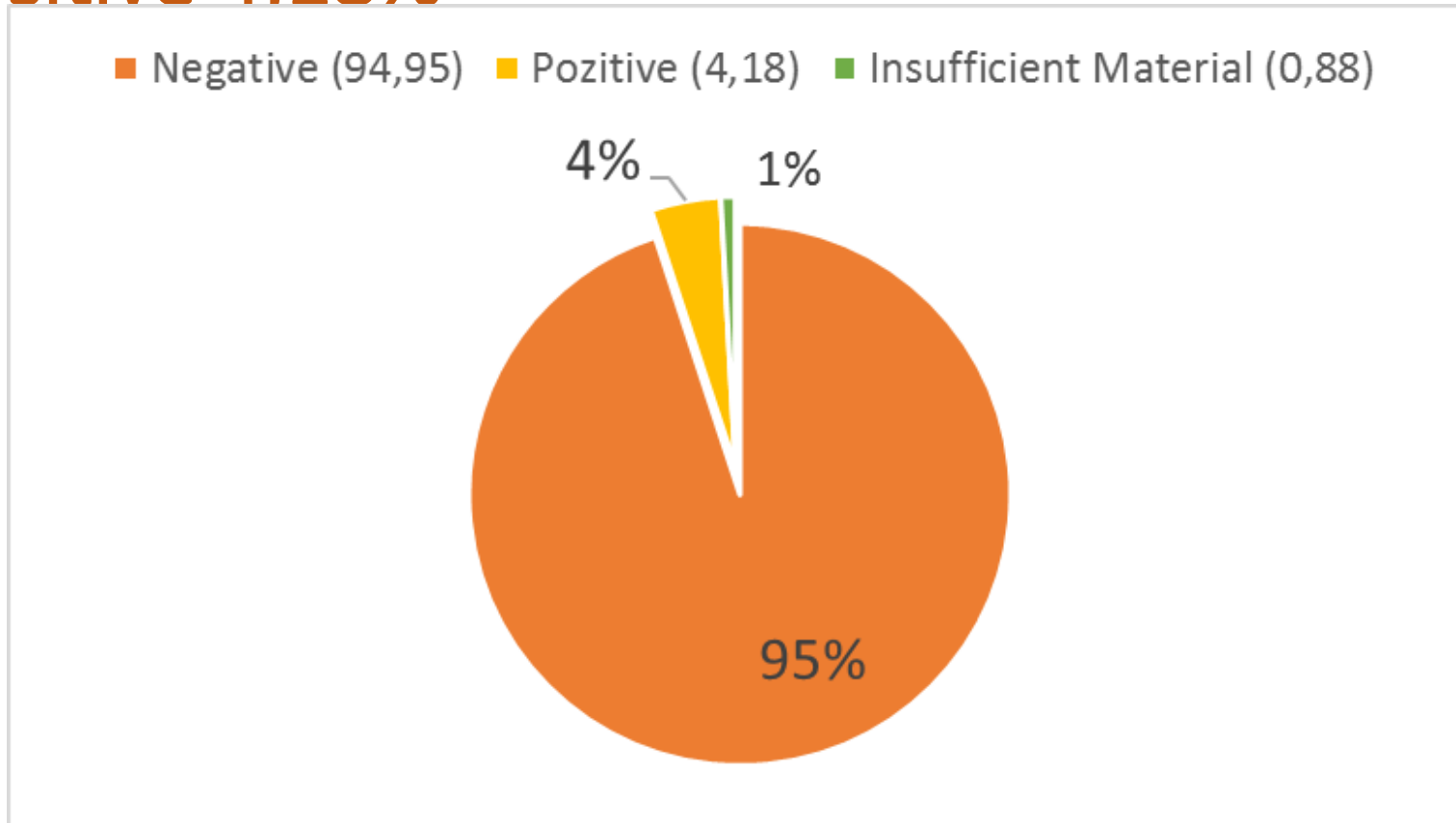


Results: Population Based Cancer Screening



HPV Test Results Global Sum (3.222.568)

Positive 4.18%



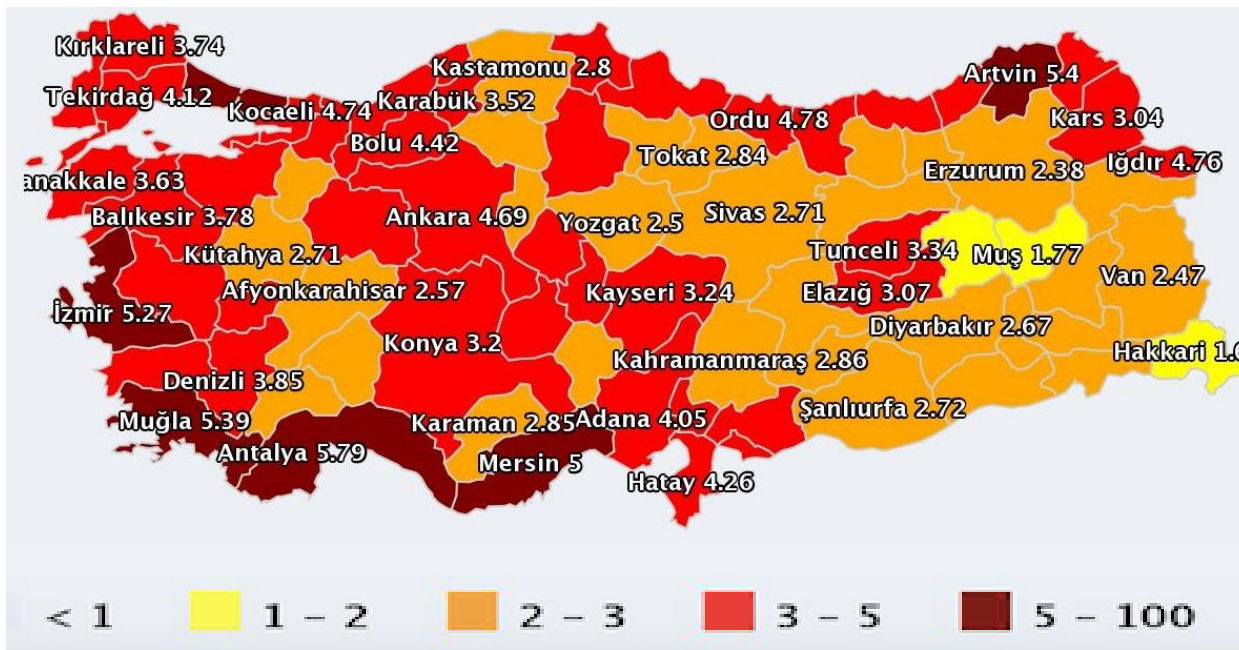
Data Acces: 20. January. 2018



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Turkish HPV Geno-Map (4,18%)



- ✓ A total of 3.200.000 were screened by HPV test.
- ✓ Approximately 12,000 abnormal smear detected (Except ASC-US)
- ✓ HPV Mapping of Turkey

Data Acces: 20. January. 2018

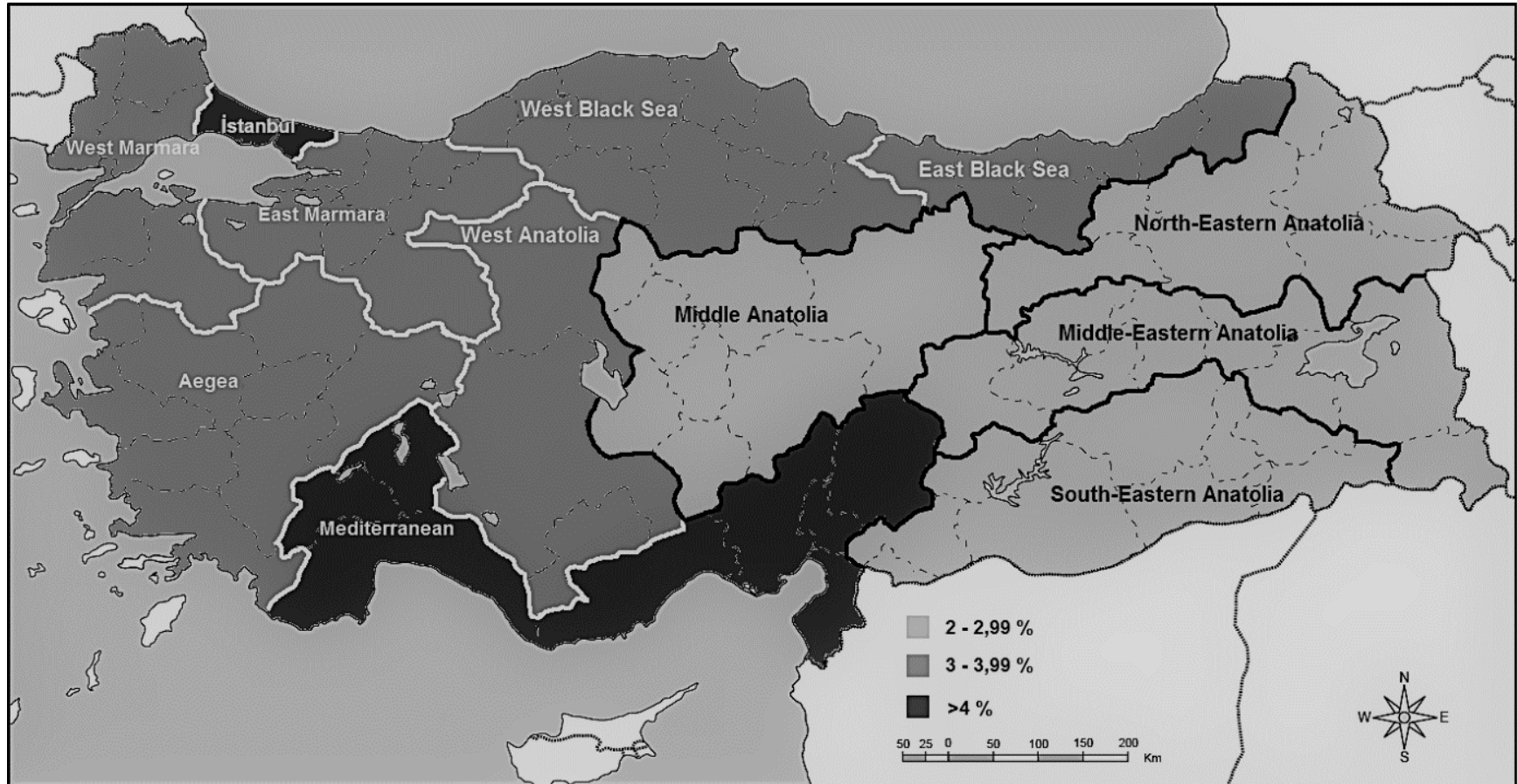


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Turkish HPV Geno-Map (4,18%)

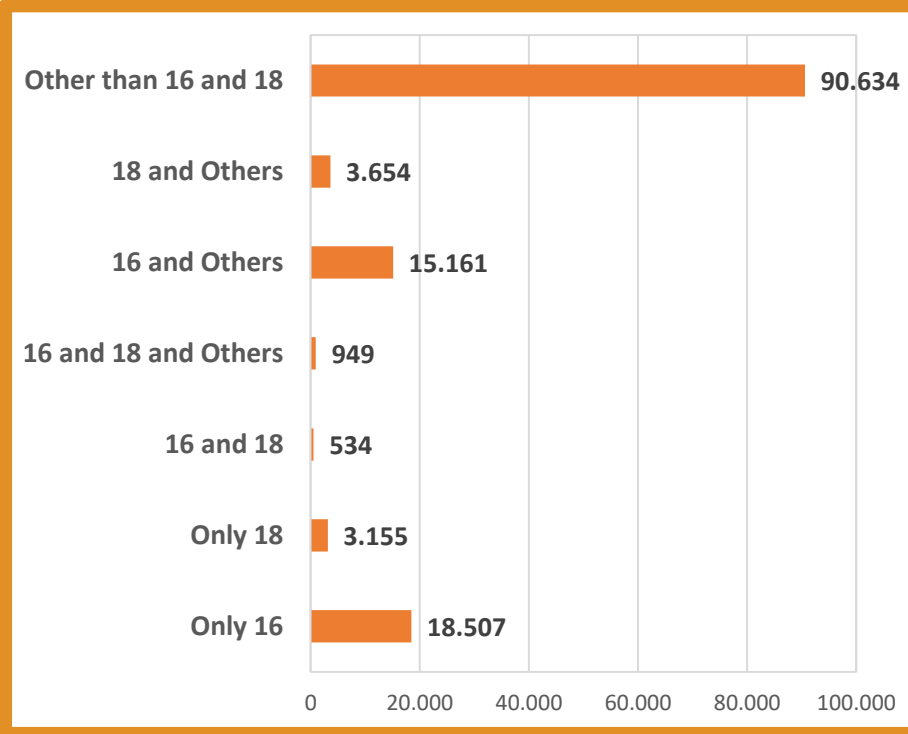
12 NUTS Bölgesi



HPV Genotypes

Total Sum (134.568)

HPV TYPES	N	%
Only 16	18.507	13,96
Only 18	3.155	2,35
16 and 18	534	0,4
16 and 18 and Others	949	0,72
16 and Others	15.161	11,44
18 and Others	3.654	2,76
Other than 16 and 18	90.634	68,38
TOTAL		100.00



Data Acces: 20. January. 2018

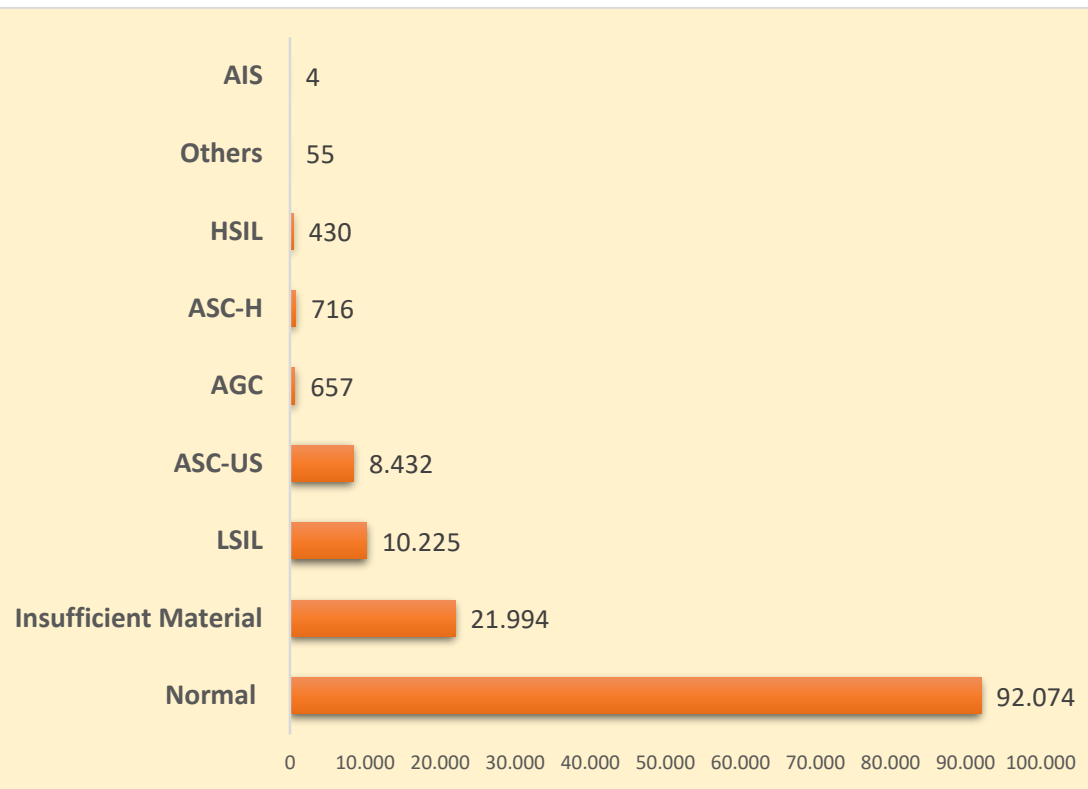


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Reflex Cytology Results (Positive 134.585)

	%
Normal	68,41
Insufficient Material	16,34
LSIL	7,60
ASC-US	6,27
AGC	0,49
ASC-H	0,53
HSIL	0,32
Others	0,04
AIS	0,00



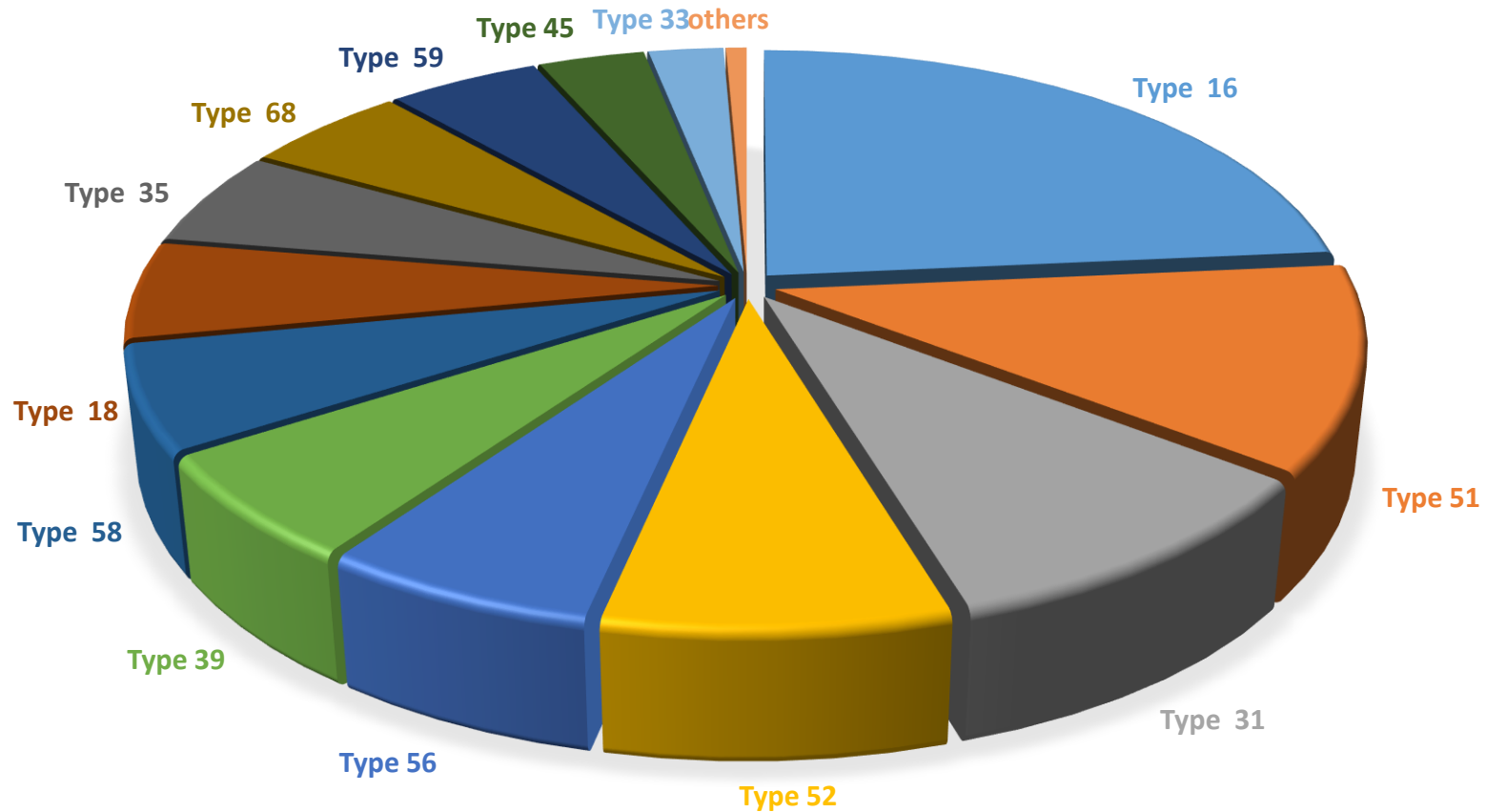
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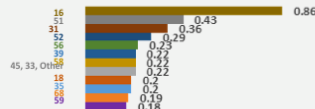
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HPV Geno-Type Distribution

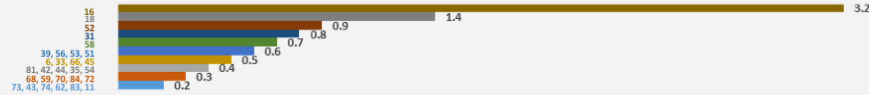


HPV Types Grouped By Their Specific Prevalence

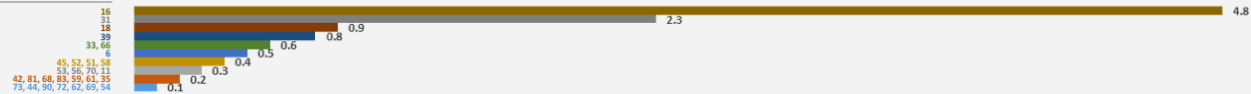
TURKEY



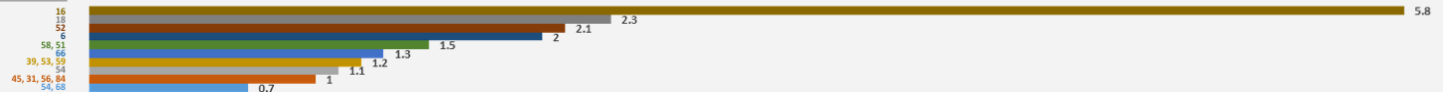
WORLD



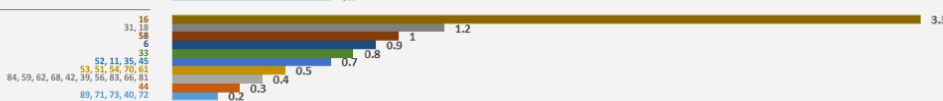
EUROPE CONTINENT



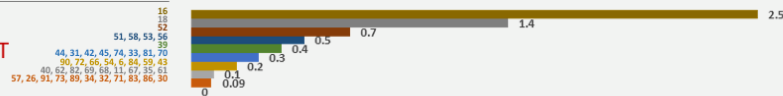
NORTHERN AMERICA



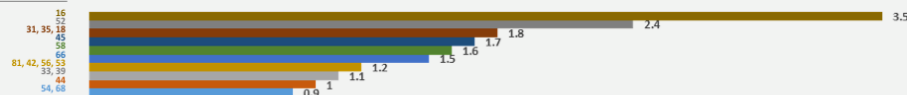
LATIN AMERICA & CARIBBEAN



ASIA CONTENT




AFRICA CONTENT



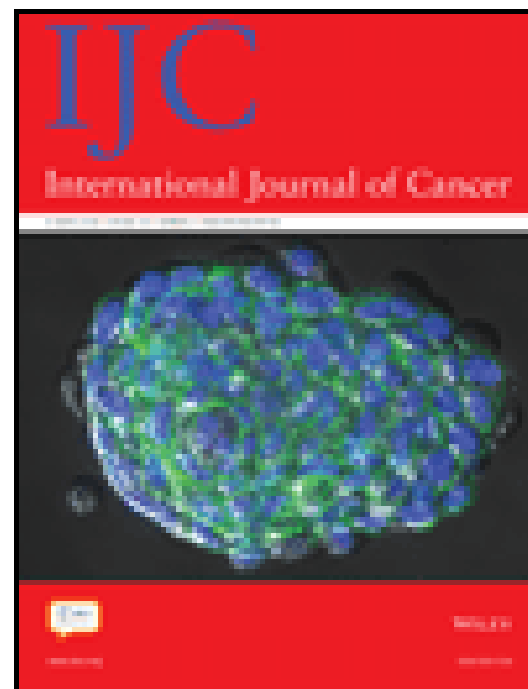
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Initial results of population based cervical cancer screening program using HPV testing in one million Turkish women

Murat Gultekin ^{1,2}, Mujdegul Zayifoglu Karaca³, Irem Kucukyildiz³, Selin Dunder³, Guledal Boztas³, Hatice Semra Turan³, Ezgi Hacikamiloglu³, Kamil Murtuza⁴, Bekir Keskinkilic³ and Irfan Sencan³

First 1 Million Patients with Colposcopy and Histology Results



Invitations, Acceptance, Attendance & Screening Rates

✓ Acceptance Rate:

- 36.5% acceptance rate for HPV DNA Screening
- This rate was 63.5% for ages 30-45y, 32.7% for ages 45-60y and 13.5% for ages 60 years and older.

✓ Attendance Rate: 82.8%.

✓ Invitation:

- | | |
|---------------------------------|-------------------------|
| ■ Telephone including SMS (60%) | 80-90% Attendance Rates |
| ■ Face to Face (30%) | 80-90% Attendance Rates |
| ■ Letter/Brochure/Social Media | 30-40% Attendance Rates |

✓ Screening Rates:

- 28.0% (30-34); 33.8% (35-39); 41.6% (40-44),
- 34.5% (45-49); 32.4% (50-54); 23.3% (55-59); 15.2% (60-65)

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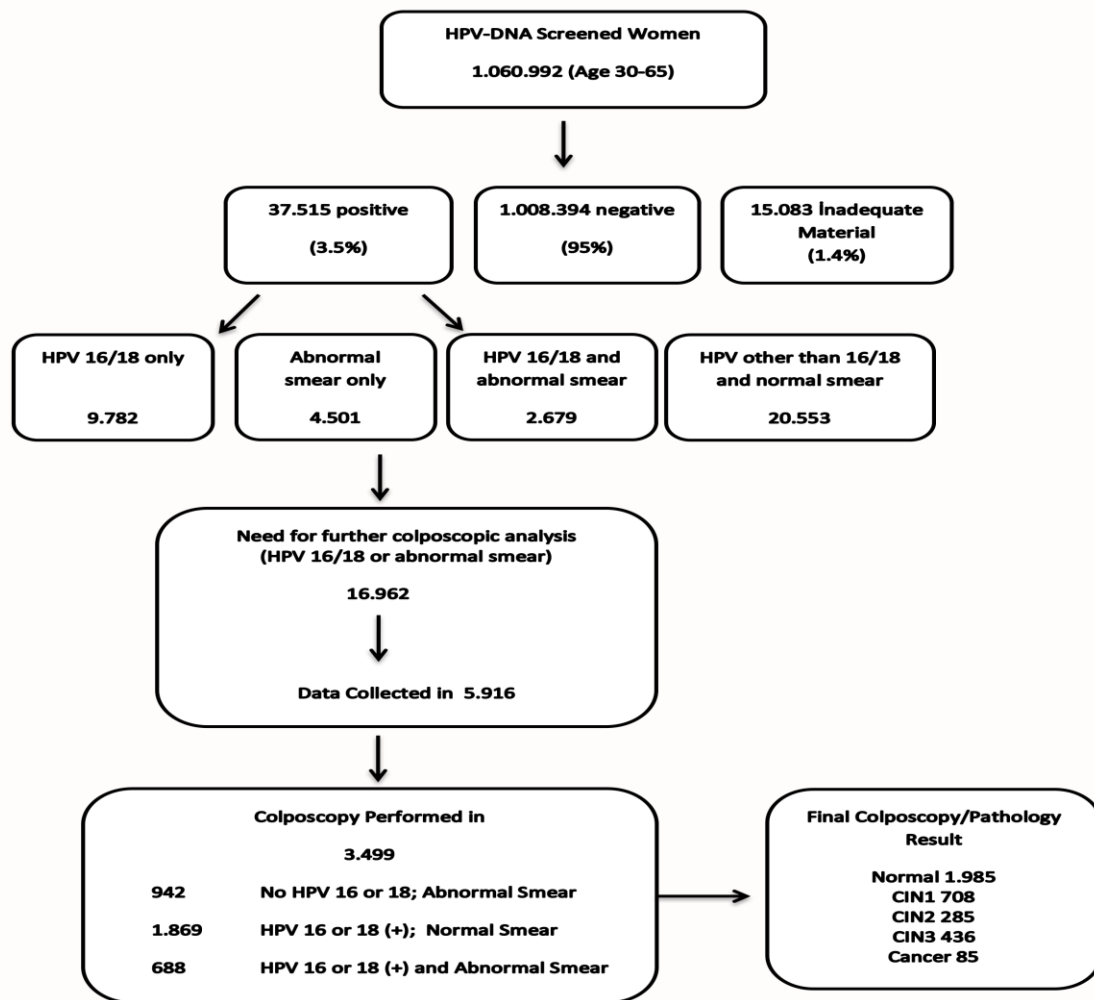
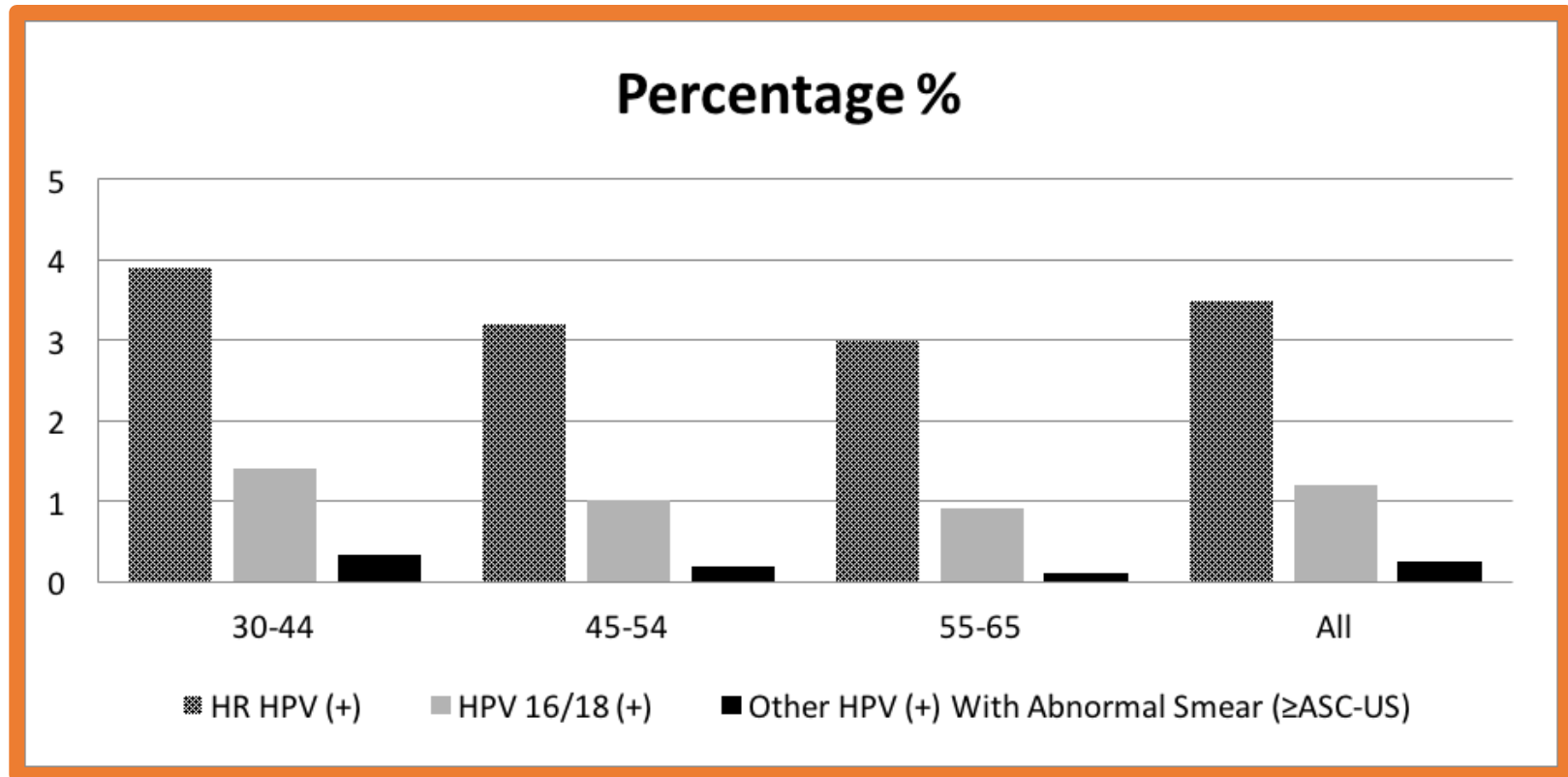


Figure 1. Study Flow Chart

DATA COMPLETENESS

- 100% at Primary Level
- 35% Secondary – Tertiary Level

HPV POSITIVITY WITHIN AGE GROUPS



HPV Genotypes among 37.515 HC2 Positive Cases (50 064 different types) by Age Groups (n, %).

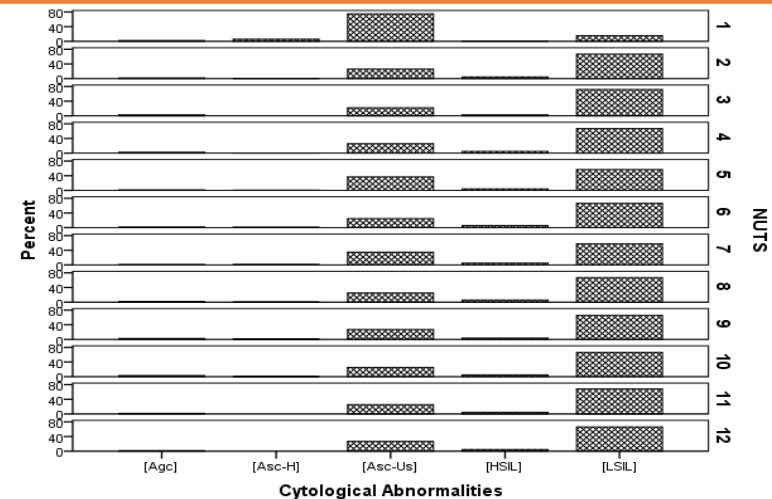
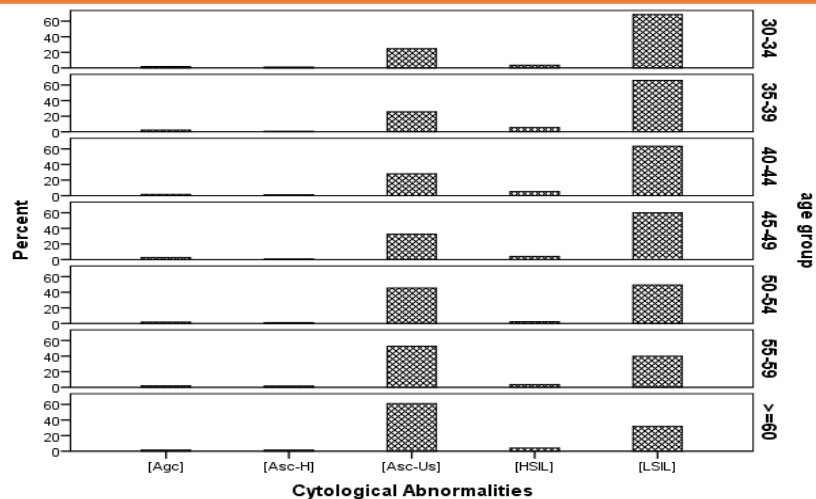
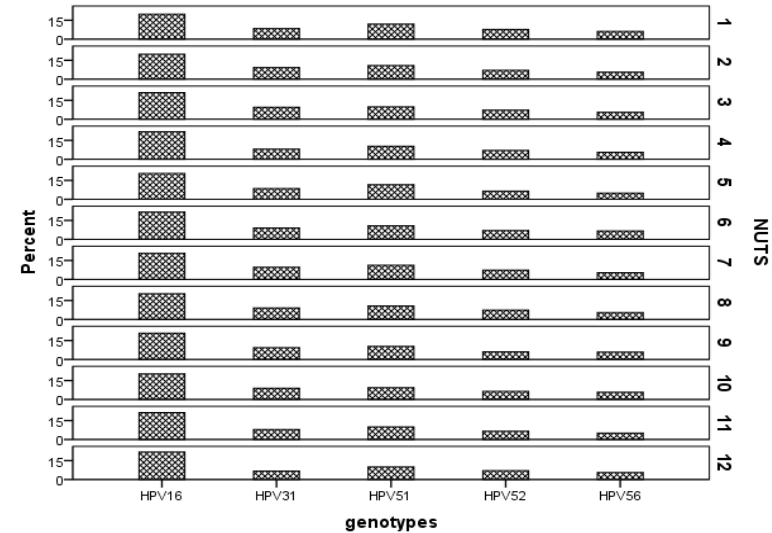
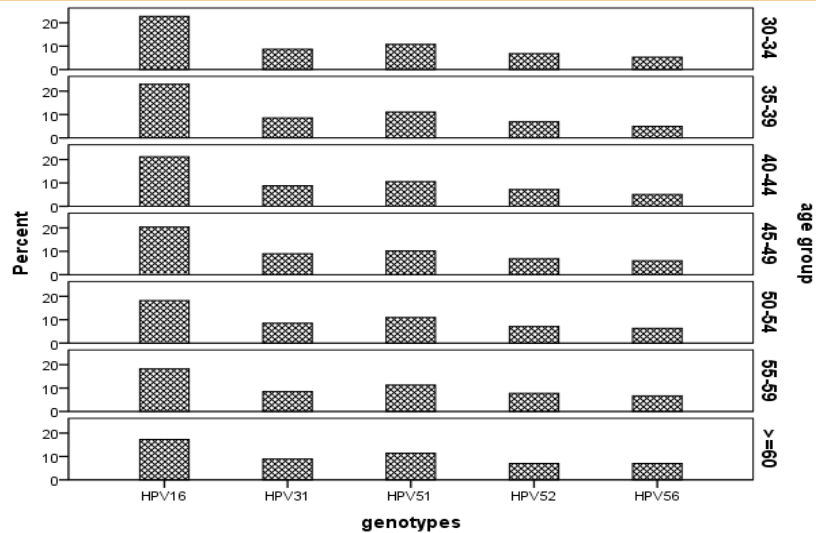
	Total		30-44	45-54	55-65
Genotype	Case	%	%	%	%
HPV16	10373	20.7	22.3	19.3	17.9
HPV18	2561	5.1	5.3	5.1	4.6
HPV31	4357	8.7	8.7	8.8	8.6
HPV33	1064	2.1	2.0	2.2	2.7
HPV35	2298	4.6	4.6	4.5	4.8
HPV39	2774	5.5	5.9	5.4	4.5
HPV45	1603	3.2	3.4	3.0	2.9
HPV51	5420	10.8	10.8	10.6	11.3
HPV52	3547	7.1	7.0	7.0	7.5
HPV56	2838	5.7	5.1	6.1	6.8
HPV58	2536	5.1	4.5	5.3	6.6
HPV59	2096	4.2	4.1	4.3	4.3
HPV68	2307	4.6	4.4	4.9	4.8
HPV73	4	0.0	0.0	0.0	0.0
Other	6286	12.6	12.0	13.6	12.7
TOTAL	50064	100	100	100	100



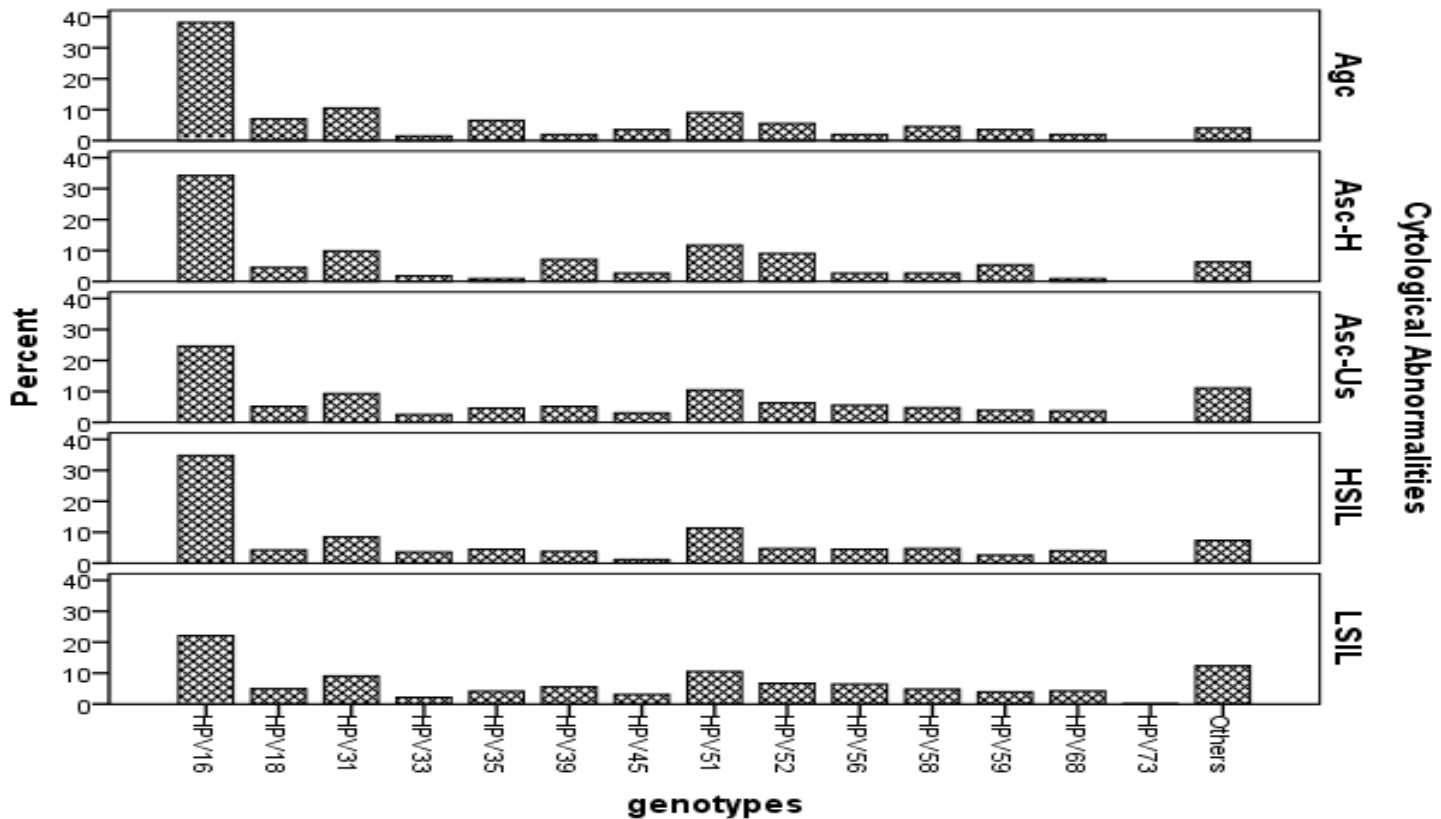
CROSS TABLES

HPV Genotypes vs. Age and NUTS Regions

Smear Abnormality vs. Age and NUTS Regions



CROSS TABLES: HPV GENOYPES VS. SMEAR ABNORMALITIES



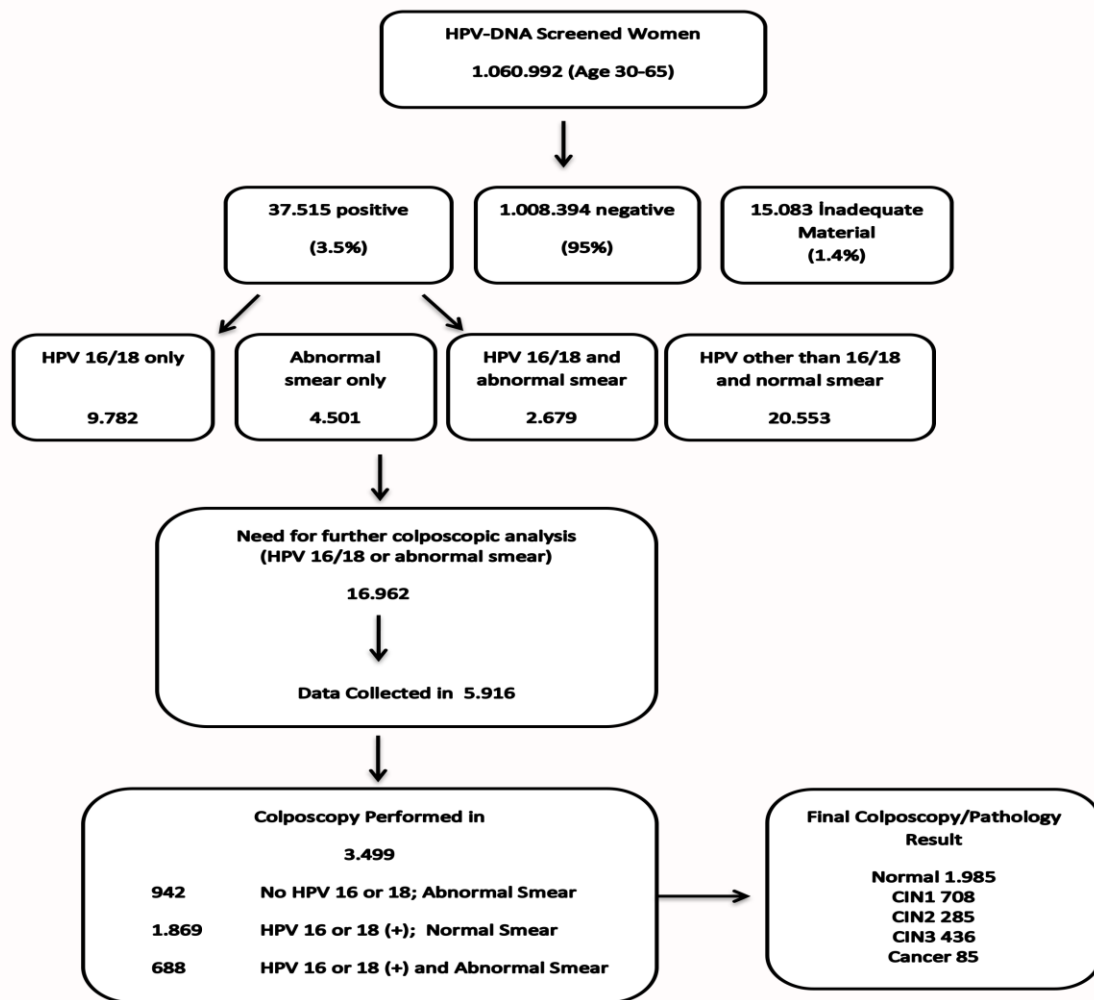
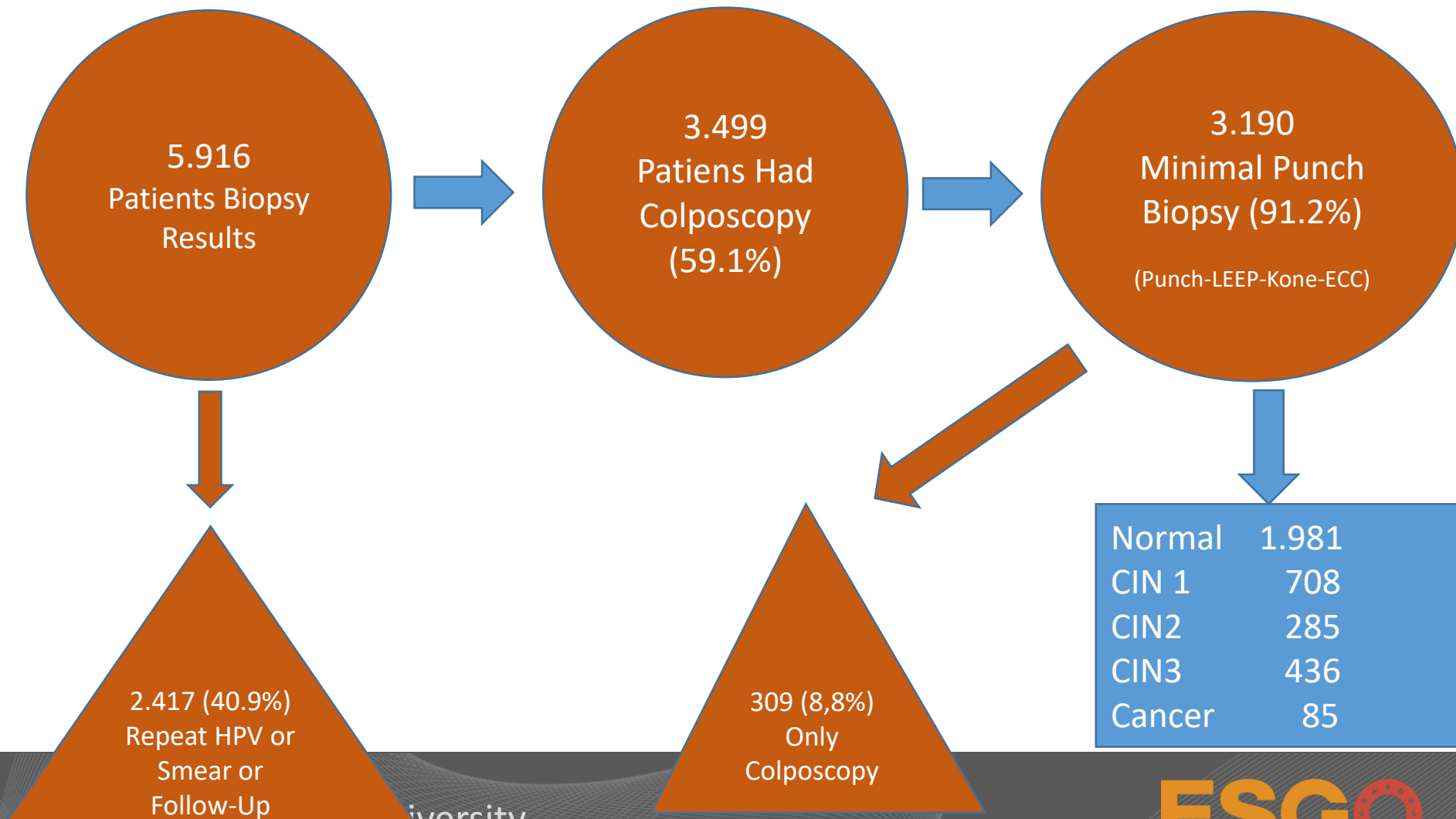


Figure 1. Study Flow Chart

DATA COMPLETENESS

- 100% at Primary Level
- 35% Secondary – Tertiary Level

Need for Colposcopy Device and Training ?



First 1 Million Results With Biopsy



- ✓ **HPV Positivity** 3,87%
 - ✓ Over 500.000 Ladies Are Carriers
- ✓ **Colposcopy Referral Rate** 1,6%
- ✓ **True positivity (CIN2+)** 23%
- ✓ **True positivity (CIN3+)** 15%
- ✓ **Cancer Incidence Over Age 30**
 - ✓ 8,0/100.000 (normal population)
 - ✓ 24/100.000 (screening population, range 8.5 - 40)
- ✓ **For CIN3+ Lesion Detection**
 - ✓ Only Cytology 52%
 - ✓ HPV Screening + 16 & 18 Genotyping 88%
- ✓ **HPV Genotyping**
 - ✓ Real bridge between continents

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ence in different regions & smear abnormalities

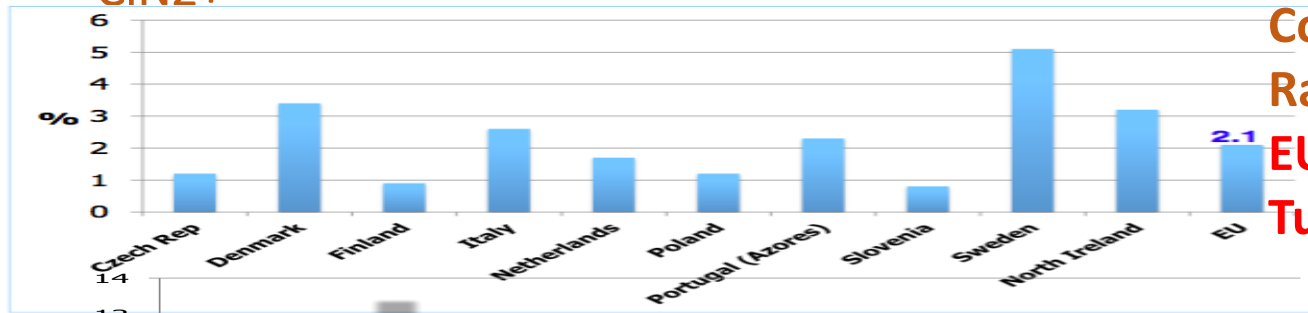


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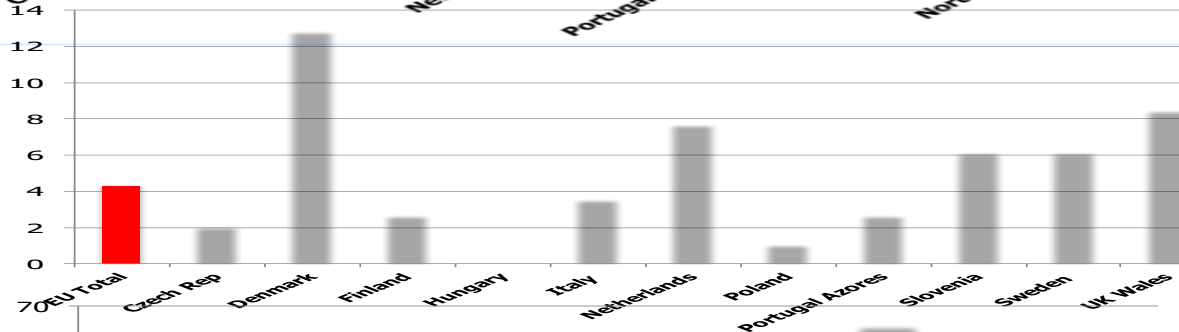
Cervical Screening : Unpublished Data

Colposcopy Referral, CIN2 Detection Rate, PPCV of Colposcopy to Detect CIN2+



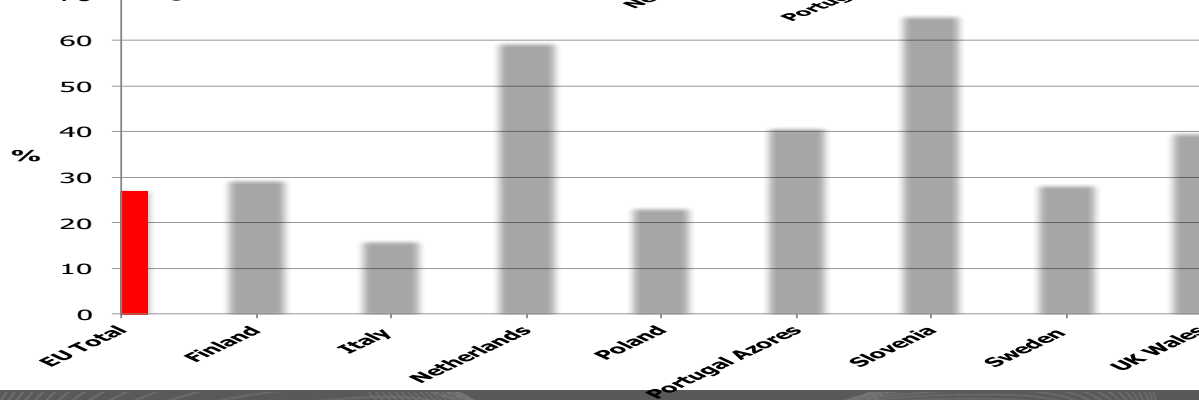
Colposcopy Referral Rates:

EU : 2.1%
Turkey : 1.6%



Cancer (CIN2+) Detection Rates Among Referred

EU : 4.0%
Turkey : 23%



PPV of Colposcopy to Detect (CIN2+)

EU : 27.0%
Turkey : 25.3%



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HPV Mega LAB Video

✓ <https://www.youtube.com/watch?v=IBmAflRjl10&t=213s>



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- ✓ Turkey is the first country in the world starting HPV screening among middle income population.
- ✓ We show that primary HPV screening is feasible within low resource settings and in conservative populations.
- ✓ However, we face challenges.



Challenges

- ✓ Resistance of cyto-pathology experts
- ✓ HPV is a sexually transmitted disease
- ✓ Resistance of GP for screening
- ✓ GP and nurses were not well trained for HPV
- ✓ HPV vaccination was not available
- ✓ Questions about adult vaccinations
- ✓ Colposcopy trainings quality and adherence to guidelines



Future for World and For Turkey

✓ World

- Netherlands, Switzerland, Sweden, Italy, UK, Germany, Australia, Canada, Denmark, Poland, Norway, Austria
- Countries with National HPV Vaccine Programs
- HPV Faster
- Urinary and Self Testing HPV
- Management of HPV Positives (ESGO –Meta-Analysis)
- ESGO ENPIGO Statement

✓ Turkey

- Screening Registry
- Colposcopy Data Follow Up System
- HPV Mobile



Thank you for your attention



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